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Association of Vascular Access Type with Inflammatory Marker Levels in Maintenance Hemodialysis Patients

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ABSTRACT

Aggressive NIH is a common histopathological lesion found at the sites of venous stenosis in arteriovenous fistula (AVF) and arteriovenous grafts (AVG). Inflammatory mediators have been proposed to play a pathogenic role in NIH, but there is paucity of data evaluating this hypothesis in clinical studies or in animal models. Serum levels of inflammatory mediators can potentially identify patients at high risk of AVF and AVG dysfunction. In a cross-sectional cohort study of 754 HD patients who were part of the NIED study cohort, we examined the associations between inflammatory markers including serum interleukin (IL) 1 β , IL-6, C-reactive protein (CRP), and tumor necrosis factor- α (TNF- α) and type of vascular access. Unadjusted and multivariate-adjusted linear regression models were used. In addition, time-dependent regression model was used to assess the association between inflammatory markers and mortality. We observed that in the multivariate-adjusted model, inflam-

matory mediators interleukin-6 (IL-6), interleukin-1L- β (IL-1 β), and C-reactive protein (CRP), the predicted value in hemodialysis patients, are lowest in patients with AVF and highest in central venous catheter (CVC) and AVG even in case-mix and malnutrition-inflammation complex syndrome (MICS)-adjusted models. IL-6 and CRP levels fall consistently in the same patients when AVG or CVC is changed to AVF and increase if the same patient changes access from AVF to AVG or CVC. Obesity is a risk factor for fistula failure and fistulas are associated with the lowest mortality compared with CVC and AVG. We did not find any statistically significant association between tumor necrosis factor- α (TNF- α) and vascular access outcomes. Higher levels of inflammatory mediators seen in CVC and AVG compared with AVF could potentially explain the higher mortality seen in patients with CVC and AVG compared with AVF.

Patients with end-stage renal disease (ESRD) receive maintenance hemodialysis (MHD) through an arterio-venous fistula (AVF), the most preferred, or arteriovenous graft (AVG), the second choice if AVF cannot be placed, or a central venous catheter (CVC), which is the least preferred (1). Vascular access (AVF, AVG, CVC) dysfunction is one of the most important sources of morbidity and mortality and contributes substantially

to the cost of ESRD care (2,3). CVC, which is associated with the greatest morbidity and mortality among the vascular accesses, is used as the initial vascular access in up to 80% of incident HD patient (4–7).

Pathophysiology of AVF and AVG failure is not fully understood and interventions to mitigate this process have largely been unsuccessful. Stenosis frequently occurs in the venous segment of the AVF most commonly due to neointimal hyperplasia (NIH) and at the vein-graft anastomosis (VGA) in AVG, impeding flow frequently resulting in failure (8–14). Failure of AVG occurs typically after initial function. Inflammatory mediators have been proposed to play a pathogenic role in NIH in both AVF and AVG, but the role they play both as predictors of access failure as well as their pathogenic role in NIH is not clearly understood. The degree of leukocyte migration has been associated with the

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level of NIH (15). Leukocyte recruitment in association with growth factors is accelerated by cytokines such as IL-1, IL-1, IL-6 and TNF-alpha (16). Vascular calcification and inflammation are intricately linked. Inflammatory mediators such as TNF-alpha can induce mineralization of calcifying vascular cells in vitro and calcium phosphate crystals could activate human monocyte-derived macrophages inducing a proinflammatory state via protein kinase C and MAP kinase pathways (17,18). This vicious cycle of inflammation and arterial calcification (likely more in AVG than AVF) could explain the association between inflammation and poor outcomes in hemodialysis patients.

High levels of inflammatory markers, which may also be associated with protein energy wasting, are common in hemodialysis (HD) patients and associated with increased mortality risk in these patients (19). The associations between inflammatory markers and type of vascular access in HD patients are not clear. Our aim was to assess the association between inflammatory markers and type of vascular access. We hypothesized that patients with CVC, AVG, and AVF reported the highest, moderate, and lowest level of inflammatory markers, respectively, and patients with AVG and CVC have higher mortality than AVF.

Subjects and Methods

Patient Population

We studied MHD patients who participated in the NIED study (20). The original NIED cohort consisted of 790 patients with vascular access data who were recruited from a population base of more than 3000 MHD outpatients treated in eight DaVita maintenance dialysis clinics in Southern California during a period of 6 years. To be included in the study, patients had to be at least 18 years old and receiving outpatient hemodialysis for at least 8 weeks. Patients were excluded if they had an acute infection or had a life expectancy of less than 6 months. The study was approved by the relevant institutional review committees and all subjects gave informed consent prior to being enrolled in the study. The medical records for each subject were thoroughly reviewed by a collaborating physician in the study. Such information as underlying kidney disease, cardiovascular disease history, and other illnesses was abstracted.

Malnutrition Inflammation Score

Using the seven components of the conventional Subjective Global Assessment of Nutrition (SGA), a semiquantitative scale with three severity levels, and combining it with three new elements (body mass index, serum albumin, and total iron binding capacity [TIBC] to represent serum transferrin) in incremental fashion, the so-called Malnutrition-Inflammation Score (MIS) with 10 components has

been created (21). Each MIS component has four levels of severity from 0 (normal) to 3 (very severe). The sum of all 10 MIS components ranges from 0 to 30 denoting increasing degrees of severity. In a prospective study in MHD patients, the MIS was compared with the conventional SGA and its refinements, anthropometry, near infrared measured body fat percentage, laboratory measures including serum C-reactive protein (CRP), and 12-month prospective hospitalization and mortality rates (21). The MIS was found to be a comprehensive scoring system with significant associations with prospective hospitalization and mortality as well as measures of nutrition, inflammation, and anemia in MHD patients, and was superior to conventional SGA and to individual laboratory values as a predictor of dialysis outcome and an indicator of MICS. In this study, MHD patients were scored by collaborating renal dietitians who were trained adequately for this purpose. To evaluate the degree of reproducibility, the MIS was reassessed randomly by a physician on a subset of 24 patients without reference to the first MIS evaluation. The correlation coefficient (r) between the two MIS assessments was 0.88 denoting a high degree of reproducibility.

Access Data

The type of access that was in use was checked and data entered every 3 months over a span of 5 years. Data pertaining to interventions related to vascular access were not obtained.

Laboratory Tests

Predialysis and postdialysis blood samples were obtained on a mid-week day that coincided with the day that the required quarterly blood drawings were obtained for testing at the DaVita dialysis facilities. Single pooled Kt/V was used to represent the weekly dialysis dose. All laboratory studies were performed by DaVita Laboratories (Deland, FL) using automated methods. Serum high sensitivity C-reactive protein (CRP) was measured using a turbidometric immunoassay (WPCI, Osaka, Japan; normal range <3.0 mg/l) (22,23). Interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF- α) levels were measured using immunoassay kits (R&D Systems, Minneapolis, MN, USA; units: pg/ml; normal range: IL-6: <9.9 pg/ml, TNF- α : <4.7 pg/ml) (24,25). The C-reactive protein (CRP), TNF- α , and IL-6 levels were measured in the General Clinical Research Center Laboratories at Harbor UCLA. Serum transthyretin (prealbumin) was measured by immunoprecipitation and plasma homocysteine concentration was measured by high performance liquid chromatography (HPLC) in the Harbor-UCLA Clinical Laboratories. Inflammatory mediators were checked every 6 months along with the type of vascular access over a 5-year period.

Statistical Methods

The NIED study was a prospective study, whereas our analyses were cross-sectional using baseline data at the inception of the cohort. Data were summarized using proportions, means (\pm standard deviation [SD]), or medians (interquartile range [IQR]) as appropriate. Categorical variables were compared using chi-square tests, and continuous variables were compared using t tests or Mann–

Whitney U tests, Kruskal–Wallis H tests, or analyses of variance, as appropriate. We used Pearson’s and Spearman’s rank order correlation coefficients for selected analyses where indicated. Multivariate regression analyses including linear and logistic regression were performed to assess the association between type of access and inflammatory/nutritional markers. In our fully adjusted model, we adjusted for age, gender, race, marital status, type of insurance, Charlson Comorbidity Index, dialysis vintage,

TABLE 1. Baseline characteristics of 790 patients with access data at baseline

	Fistula	Graft	Catheter	<i>p</i> for trend	ANOVA
<i>N</i>	324	312	154	N/A	N/A
Age (years) (mean \pm SD)	51 \pm 15	55 \pm 14	53 \pm 16	0.025	0.001
Gender (men%)	66	46	44	0.44	<0.001
Ethnicity (Hispanics%)	61	42	54	0.001	<0.001
Race (Blacks%)	21	40	30	0.001	<0.001
Dialysis vintage (months) (median (IQR))	20.7 (8.7–41.5)	26.8 (11.5–52.6)	5.4 (2.6–16.1)	<0.001	<0.001
BMI (kg/m ²) (mean \pm SD)	25.4 \pm 5.2	27.3 \pm 6.5	27.0 \pm 7.0	0.029	<0.001
nPCR (g/kg/day) (mean \pm SD)	1.09 \pm 0.24	1.05 \pm 0.22	1.07 \pm 0.27	0.24	0.80
History of cardiac disease (%)	25	38	29	0.015	0.003
Charlson comorbidity score (median (IQR))	2 (0–3)	2 (0–3)	2 (1–3)	0.003	<0.001
Malnutrition–inflammation score (median (IQR))	4 (2–6)	4 (3–7)	6 (3–8)	0.08	<0.001
Laboratory results					
Serum C-reactive protein (mg/dl) (median (IQR))	3.1 (1.2–6.7)	4.3 (1.6–7.9)	3.9 (1.7–7.9)	0.79	0.018
Ln transformed serum C-reactive protein (mg/dl) (median (IQR))	1.18 (0.22–1.86)	1.43 (0.51–2.06)	1.30 (0.54–2.02)	0.78	0.01
Serum IL1beta (pg/ml) (median (IQR))	0.34 (0.16–0.84)	0.41 (0.19–0.79)	0.61 (0.23–1.61)	0.04	0.002
Ln transformed serum IL1beta (pg/ml) (median (IQR))	−1.08 (−1.83 to −0.17)	−0.89 (−1.66 to −0.24)	−0.49 (−1.47 to −0.48)	0.04	0.008
Serum IL6 (pg/ml) (median (IQR))	5.6 (3.4–11.5)	7.9 (4.5–14.1)	8.9 (4.7–16.2)	0.72	0.17
Ln transformed serum IL6 (pg/ml) (mean \pm SD)	1.89 \pm 1.01	2.15 \pm 0.96	2.25 \pm 1.03	0.71	<0.001
Serum TNF-alpha (pg/ml) (median (IQR))	5.4 (3.9–8.6)	6.3 (4.0–9.2)	5.4 (3.3–9.0)	0.08	0.16
Ln transformed serum TNF-alpha (pg/ml) (mean \pm SD)	1.77 \pm 0.71	1.82 \pm 0.72	1.77 \pm 0.91	0.07	0.64
Serum albumin (g/dl) (mean \pm SD)	4.01 \pm 0.35	3.85 \pm 0.36	3.76 \pm 0.42	0.82	<0.001
Blood hemoglobin (g/dl) (mean \pm SD)	12.2 \pm 1.0	12.2 \pm 0.9	12.1 \pm 1.1	0.26	0.11
Iron saturation ratio (%) (mean \pm SD)	33 \pm 11	32 \pm 10	31 \pm 12	0.86	0.19
TIBC (mg/dl) (mean \pm SD)	212 \pm 40	202 \pm 37	212 \pm 41	0.001	0.003
Serum prealbumin (mg/dl) (mean \pm SD)	29.5 \pm 9.8	27.6 \pm 8.8	27.5 \pm 10.5	0.97	0.043
Serum creatinine (mg/dl) (mean \pm SD)	10.5 \pm 3.4	10.3 \pm 3.1	9.0 \pm 3.1	0.001	<0.001
Intact PTH (μ m/l) (median (IQR))	212 (132–364)	209 (129–371)	199 (118–302)	0.30	0.88
White blood cells (10 ⁹ cell/l) (mean \pm SD)	7.0 \pm 2.1	7.2 \pm 2.4	7.8 \pm 2.4	0.29	0.004
Peripheral lymphocyte count (%) (mean \pm SD)	24 \pm 8	22 \pm 8	22 \pm 8	0.23	0.003

center, Kt/V, residual renal function, nPCR, BMI, blood hemoglobin, serum albumin, phosphate, TIBC, ferritin, bicarbonate, calcium, and white blood cells.

To assess the association between different type of access and mortality, time-dependent Cox regression model was used. We censored for kidney transplantation and lost of follow-up. Data analysis was performed using STATA version 11.1 (STATA Corporation, College Station, TX).

Results

Baseline Characteristics

Mean age (\pm SD) of patients was 53 ± 15 years; 54% of patients ($n = 425$) were men, 52% ($n = 411$) were Hispanic, 30% ($n = 240$) were African-American, and 53% ($n = 415$) were diabetic. At the baseline, 41%, 39%, and 20% of patients had fistula, graft, and catheter, respectively. The mean dialysis vintage was 30 ± 32 months (median: 19, interquartile range: 7–42 months). The average (mean \pm SD) baseline serum albumin in the 790 MHD patients was 3.90 ± 0.38 ng/ml.

Table 1 shows baseline demographic, clinical, and laboratory variables according to the 3 baseline access categories in 790 maintenance hemodialysis patients. Patients with fistula were younger, more likely to be male, less likely to be Black, and less likely to have cardiac disease. In addition, patients with fistula had lower serum CRP, IL1beta, and IL6 level.

Table 2 shows the association between different type of access and serum level of inflammatory markers. Compared with fistula, having catheter was significant predictor of IL1 beta level in

unadjusted model. After adjustment for important covariables, having catheter remained significant and independent predictor. Figure 1 shows the predicted value of serum IL1 beta level based on multivariate linear regression analysis. Patients with catheter had significantly higher level of predicted serum IL1 beta level than patients with fistula. Figure 2 shows the predicted value of serum CRP level based on multivariate linear regression analysis. Patients with catheter had significantly higher level of predicted serum CRP level than patients with fistula in our case-mix-adjusted model. Figure 3 shows the predicted value of serum IL6 level based on multivariate linear regression analysis. Patients with catheter had significantly higher level of predicted serum IL6 level than patients with fistula in our case-mix and MICS-adjusted model. In addition, catheter use was a significant and independent predictor of serum IL6 level after adjustment for important covariables (Table 2). Figure 4 shows the predicted value of serum TNF-alpha level based on multivariate linear regression analysis. There was no association between TNF-alpha level and type of access.

The association of type of access with the mortality is shown in Table 3. Compared with patients with fistula, patients with graft and catheter had 46% (HR: 1.46, 95% CI: 1.07–1.99) and 125% (HR: 2.25, 95% CI: 1.46–3.49) higher all-cause mortality. After additional adjustment for case-mix and MICS variables, patients with fistula had 73% (HR: 1.73, 95% CI: 1.07–2.79) higher death risk compared with patients with fistula (Table 4).

Figure 5 shows the difference between baseline+6 months serum CRP level and baseline serum CRP level in different subgroups of patients. The CRP level did not change in patients who remained in

TABLE 2. Linear regression models of serum inflammatory cytokines levels and type of access in unadjusted, case-mix-adjusted and case-mix and MICS-adjusted models

	Unadjusted			Case-mix-adjusted*			Case-mix and MICS-adjusted**		
	Coefficient	95% CI of coefficient	<i>p</i> -value	Coefficient	95% CI of coefficient	<i>p</i> -value	Coefficient	95% CI of coefficient	<i>p</i> -value
Dependent variable: Ln Interleukin 1 beta									
Fistula		Reference			Reference			Reference	
Graft	−0.017	−0.396; 0.362	0.93	0.027	−0.388; 0.442	0.90	−0.056	−0.469; 0.357	0.79
Catheter	0.609	0.183; 1.036	0.005	0.618	0.154; 1.082	0.009	0.590	0.127; 1.053	0.013
Dependent variable: Ln Interleukin 6									
Fistula		Reference			Reference			Reference	
Graft	0.255	0.100; 0.409	0.001	0.117	−0.041; 0.275	0.15	0.044	−0.109; 0.198	0.57
Catheter	0.355	0.164; 0.546	<0.001	0.406	0.215; 0.598	<0.001	0.279	0.091; 0.467	0.004
Dependent variable: C-reactive protein									
Fistula		Reference			Reference			Reference	
Graft	0.199	0.035; 0.363	0.018	0.094	−0.079; 0.267	0.29	0.025	−0.140; 0.190	0.77
Catheter	0.276	0.073; 0.479	0.008	0.237	0.027; 0.446	0.027	0.150	−0.052; 0.352	0.15
Dependent variable: Ln Tumor Necrosis Factor alpha									
Fistula		Reference			Reference			Reference	
Graft	0.052	−0.066; 0.169	0.39	0.030	−0.093; 0.154	0.63	0.025	−0.099; 0.150	0.69
Catheter	−0.001	−0.147; 0.144	0.99	0.042	−0.107; 0.192	0.58	0.036	−0.117; 0.188	0.64

*Case-mix models adjusted for: age, gender, race, marital status, type of insurance, Charlson Comorbidity Index, dialysis vintage, center, Kt/V, and residual renal function.

**Case-mix and MICS models adjusted for: variables in case-mix models and nPCR, BMI, blood hemoglobin, serum albumin, phosphate, TIBC, ferritin, bicarbonate, calcium, and white blood cells.

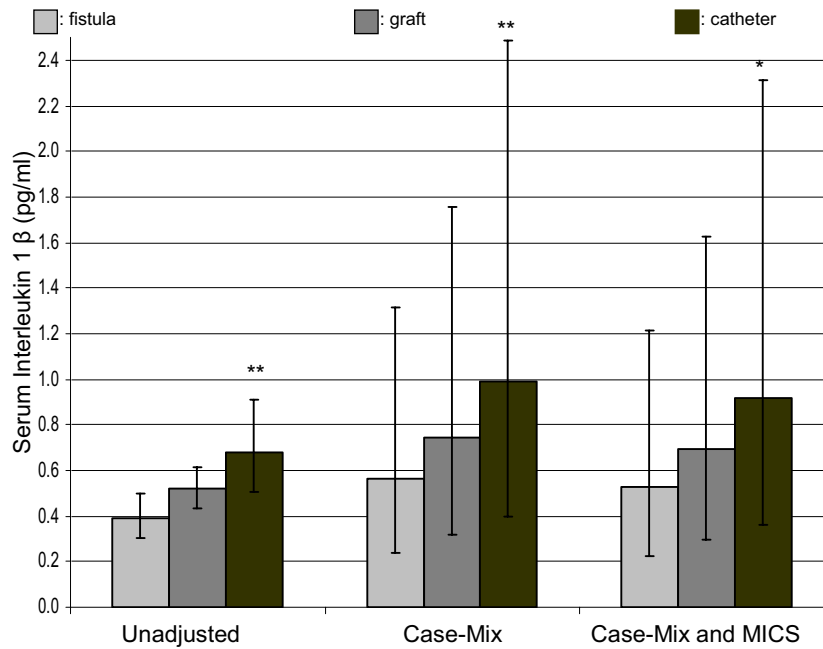


FIG. 1. Unadjusted, case-mix-adjusted and case-mix and MICS-adjusted serum interleukin 1 β levels (95% confidence intervals) in patients divided along type of access. Case-mix models adjusted for: age, gender, race, marital status, type of insurance, Charlson Comorbidity Index, dialysis vintage, center, Kt/V, and residual renal function. Case-mix and MICS models adjusted for: variables in case-mix models and nPCR, BMI, blood hemoglobin, serum albumin, phosphate, TIBC, ferritin, bicarbonate, calcium, and white blood cells. Comparisons were made in linear regression models, with the group of fistula access as referent. * $p < 0.05$, ** $p < 0.01$.

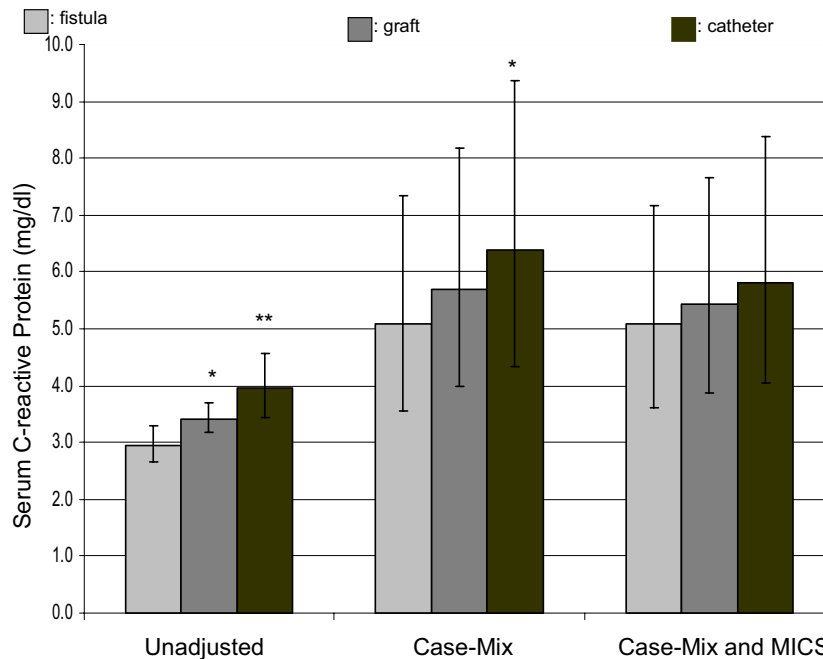


FIG. 2. Unadjusted, case-mix-adjusted and case-mix and MICS-adjusted serum C-reactive protein levels (95% confidence intervals) in patients divided along type of access. Case-mix models adjusted for: age, gender, race, marital status, type of insurance, Charlson Comorbidity Index, dialysis vintage, center, Kt/V, and residual renal function. Case-mix and MICS models adjusted for: variables in case-mix models and nPCR, BMI, blood hemoglobin, serum albumin, phosphate, TIBC, ferritin, bicarbonate, calcium, and white blood cells. Comparisons were made in linear regression models, with the group of fistula access as referent. * $p < 0.05$, ** $p < 0.01$.

the same access type during this period. However, changing access from fistula to graft increased, while changing access from graft to fistula decreased the serum CRP level (Fig. 5).

Figure 6 shows the difference between baseline+6 months serum IL6 level and baseline serum IL6 level in different subgroups of patients. The serum IL6 level did not change in patients who remained

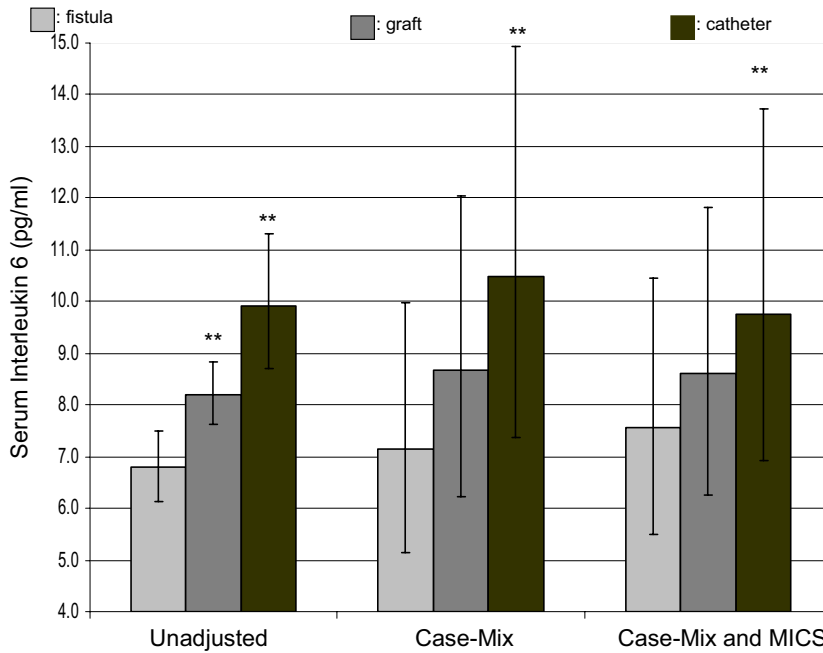


FIG. 3. Unadjusted, case-mix-adjusted and case-mix and MICS-adjusted serum interleukin 6 levels (95% confidence intervals) in patients divided along type of access. Case-mix models adjusted for: age, gender, race, marital status, type of insurance, Charlson Comorbidity Index, dialysis vintage, center, Kt/V, and residual renal function. Case-mix and MICS models adjusted for: variables in case-mix models and nPCR, BMI, blood hemoglobin, serum albumin, phosphate, TIBC, ferritin, bicarbonate, calcium, and white blood cells. Comparisons were made in linear regression models, with the group of fistula access as referent. * $p < 0.05$, ** $p < 0.01$.

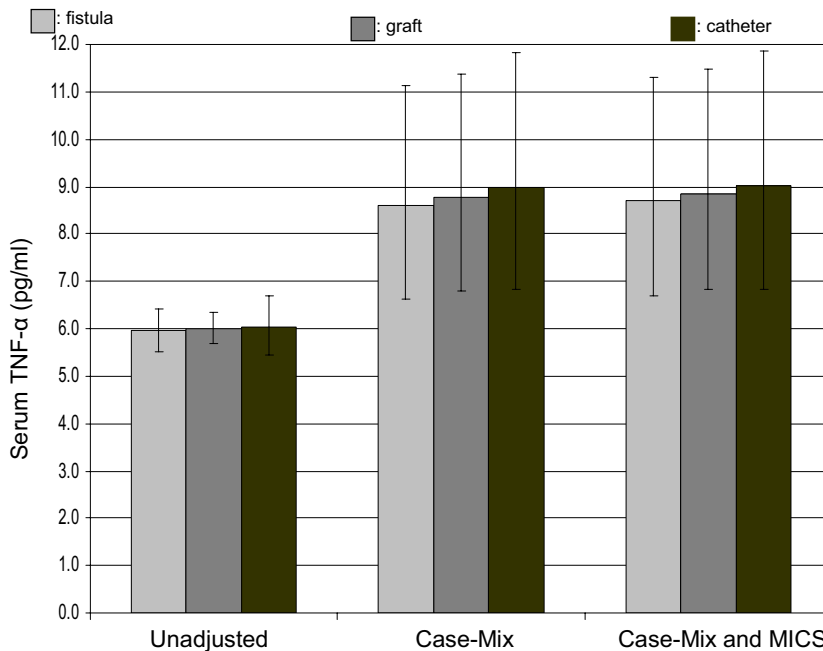


FIG. 4. Unadjusted, case-mix-adjusted and case-mix and MICS-adjusted serum tumor necrosis factor α levels (95% confidence intervals) in patients divided along type of access. Case-mix models adjusted for: age, gender, race, marital status, type of insurance, Charlson Comorbidity Index, dialysis vintage, center, Kt/V, and residual renal function. Case-mix and MICS models adjusted for: variables in case-mix models and nPCR, BMI, blood hemoglobin, serum albumin, phosphate, TIBC, ferritin, bicarbonate, calcium, and white blood cells. Comparisons were made in linear regression models, with the group of fistula access as referent. * $p < 0.05$, ** $p < 0.01$.

in the same access type during this period. However, changing access from fistula to catheter increased, while changing access from catheter to fistula decreased the serum IL6 level (Fig. 6).

Discussion

In this cross-sectional analysis of 790 maintenance hemodialysis patients with extensive data of

TABLE 3. Death hazard ratio (and 95% confidence intervals) of mortality in graft and catheter groups compared with fistula (as reference) in our unadjusted, case-mix-adjusted and case-mix and MICS-adjusted time-dependent Cox model

	Unadjusted			Case-mix-adjusted*			Case-mix and MICS-adjusted**		
	HR	95% CI of HR	p-value	HR	95% CI of HR	p-value	HR	95% CI of HR	p-value
Fistula		Reference			Reference			Reference	
Graft	1.46	1.07–1.99	0.017	1.26	0.90–1.76	0.19	1.15	0.81–1.62	0.45
Catheter	2.25	1.46–3.49	<0.001	2.12	1.34–3.16	0.001	1.73	1.07–2.79	0.026

*Case-mix models adjusted for: age, gender, race, marital status, type of insurance, Charlson Comorbidity Index, dialysis vintage, center, Kt/V, and residual renal function.
 **Case-mix and MICS models adjusted for: variables in case-mix models and nPCR, BMI, blood hemoglobin, serum albumin, phosphate, TIBC, ferritin, bicarbonate, calcium, and white blood cells.

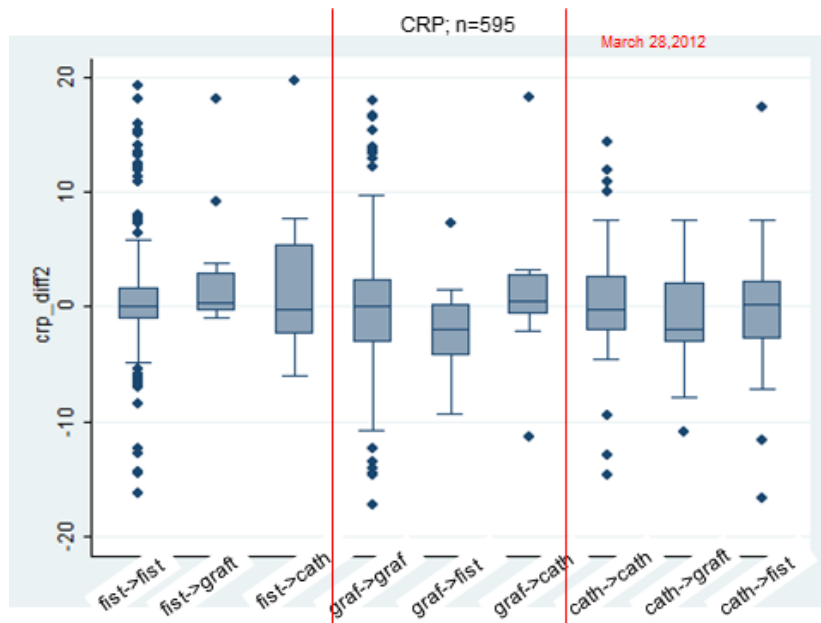


FIG. 5. Difference between baseline+ 6 months serum CRP level and baseline serum CRP level in different subgroups of patients.

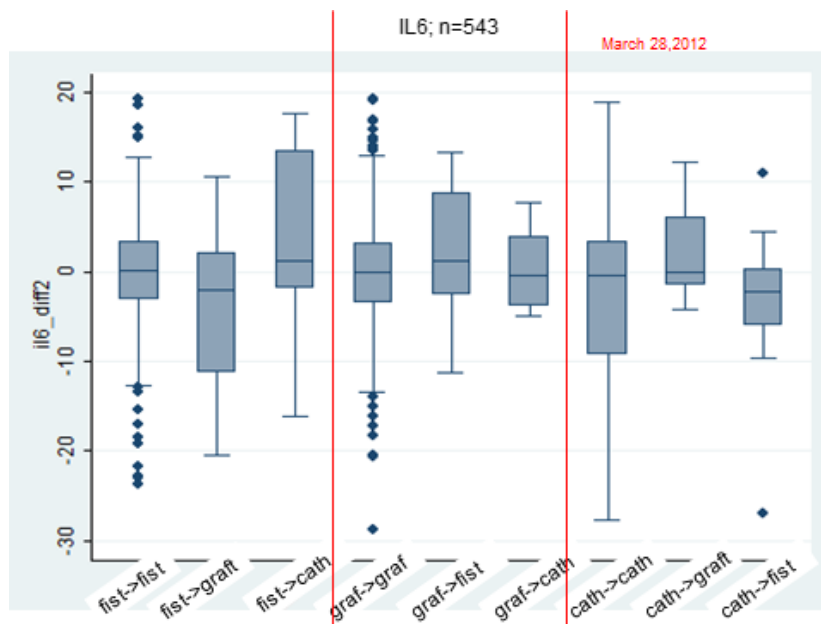


FIG. 6. Difference between baseline+ 6 months serum IL6 level and baseline serum IL6 level in different subgroups of patient.

inflammatory markers, we found that some inflammatory mediators (IL-6 and IL-1 β) were significantly higher in patients with CVC compare with patients with AVF even in case-mix and MICS-adjusted models.

Interleukin-6 (IL-6) is secreted from adipocytes and other cells within adipose tissue and act on the liver to stimulate production of large number of acute phase reactants including C-reactive protein (CRP) (26,27). CRP participates in the complement-mediated removal of damaged vascular cells and may directly be involved in the pathogenesis of neo-intimal hyperplasia (28). IL-6 and CRP have been shown to be strong predictors of cardiovascular risk (29,30). T-lymphocytes, which release cytokines such as tumor necrosis factor alpha (TNF- α), stimulate smooth muscle cell proliferation and fibroblast migration (31,32). Inhibitors of TNF- α have been shown to attenuate this response (33). TNF- α also promotes endothelial cell dysfunction.

The goal of this study was to study the association of inflammatory mediators (IL-1, IL-1 β , CRP, TNF- α) with different types of vascular access, study the interaction of obesity with fistula survival, and compare mortality among AVF, AVG, and CVC. We observed that the inflammatory mediators (IL-6, IL-1 β , and CRP) in hemodialysis patients are lowest in patients with AVF and highest in CVC and AVG even in case-mix and MICS-adjusted models. IL-6 and CRP levels fall consistently in the same patients when AVG or CVC is changed to AVF and increase if the same patient changes access from AVF to AVG or CVC.

Obesity has been shown to be a risk factor for lower prevalence of functioning AVF (34–36). Obesity is a risk factor for fistula failure (37,38). In this study, we show that obesity increases the risk of having an AVG or CVC.

Fistulas were associated with the lowest mortality compared with CVC and AVG. We did not find any statistically significant association between TNF- α and vascular access outcomes. A prospective study with serial measurement of inflammatory mediators and recording of vascular access interventions will help us determine the pathophysiological role of these inflammatory mediators in the pathogenesis of fistula failure. Measurement of inflammatory mediator(s) on routine blood test has the potential to identify patients at high risk of fistula failure and prevent fistula failure with preemptive intervention.

This study has some limitations. First, this study was done retrospectively with no data on interventions required or performed in these patients and therefore there is no data on the temporal association between rise or fall of inflammatory mediators and the endovascular intervention performed. Second, this study had inflammatory mediators checked only every 6 months, although was checked over a 5-year period. Third, as we do not have data on hospitalizations in this cohort, the correlation of inflammatory mediators to hospitalization-related illness could not be examined.

The strength of the study is the large number of subjects studied longitudinally over 5 years with inflammatory mediators and their association with type of vascular access, body mass index, and mortality.

Conclusion

In summary, we conclude that inflammatory mediators (IL-6 and IL-1 β) were significantly higher in patients with CVC compare with patients with AVF even in case-mix and MICS-adjusted models. Fistulas were associated with the lowest mortality compared with CVC and AVG. We did not find any statistically significant association between TNF- α and vascular access outcomes. The association between types of dialysis access and inflammatory markers may be the underlying link between vascular access and mortality differential and warrant additional studies.

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